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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FREDMAN, JEFFREY NORMAN	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 07/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/660,122	ECKER ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 May 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-27,30-34 and 44-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-27,30-34 and 44-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status

1. Claims 23-27, 30-34 and 44-55 are pending.

Claims 23-27, 30-34 and 44-55 are rejected.

Any rejection which is not reiterated in this action is hereby withdrawn as no longer applicable.

Claim Interpretation

2. The term "measuring base composition" in claim 30 can be interpreted in several different ways. Any analysis of a PCR product which provides the molecular mass of the PCR product, where the template sequence is known, measures one aspect of the "base composition" of the amplification product, which is the size of the product. Applying this interpretation, Jurinke teaches the claimed "measuring" step. The claim does not require specific identifying the number of each type of base in the analysis, but simply requires measuring some aspect of "base composition".

Claim Rejections - 35 USC § 112

3. Claim 27 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

As MPEP 2163.06 notes " If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen , 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)."

Here, claim 27 incorporates what is apparently new matter. While the specification discusses electrospray ionization, that is never combined with "time of flight". No specific support was identified for this limitation. Since no basis has been found to support the new claim limitation in the specification, the claim is rejected as incorporating new matter.

Further, since the parent specifications also do not support this limitation, this claim is not accorded priority to any parent application.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 23-26, 30-34, 45-48 and 51-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jurinke et al (Genetic Analysis: Biomolecular Engineering (1996) 13:67-71) in view of Norder et al (J. Med. Virol. (1990) 31:215-221).

Jurinke teaches a method of claims 23 and 30 of providing viral bioagent characterizing information (see abstract), comprising:

(a) *amplifying nucleic acid from said virus with a pair of primers to conserved regions of a housekeeping gene that is conserved among members of a viral family to produce an amplification product* (see page 68, where primers were selected in the highly conserved regions of the HBV genomes and where RT-PCR was performed on virus solutions),

wherein the amplification product corresponds to a bioagent identifying amplicon (see page 256, figure 1, where the amplification products are detected)

(b) *measuring the molecular mass of said amplification product by mass spectrometry* (see page 68, subheading "MALDI-TOF MS", where Jurinke measures the molecular mass with mass spectrometry).

(c) *comparing the molecular mass of the amplification product with known molecular masses of known bioagent identifying amplicons of members of said viral family wherein a match of molecular mass of the amplification product with a known mass of a known bioagent identifying amplicon of a member of the viral family indicates*

the identity of the virus (see page 70, where the mass of sample 1 is compared to sample 3 to demonstrate the presence of HBV in the sample).

With regard to claims 25, 32, HBV are threat agents (see abstract) (also see page 36 of the specification which lists Hepatitis viruses as biological warfare threat agents).

With regard to claims 26, 33, Jurinke suggests detection of different subtypes (see page 71, column 1, "determining different HBV subtypes by different masses of the HBV related PCR products").

With regard to claims 48 and 54, Jurinke teaches detection of the HBV core antigent (see page 69, column 1, paragraph 2).

With regard to claims 45-47 and 51-53, Jurinke expressly suggests detection of HIV and HCV, where HCV is a member of the Flaviviridae family (see page 67, column 1).

Jurinke suggests analysis of subtypes but does not exemplify detection of four members of the HBV viral family.

Norder teaches typing of 8 subtypes of HBV by PCR (see page 219, figure 2, for example).

With regard to claim 24, Norder expressly teaches measuring with multiple pairs of primers (see figure 2 and page 216, column 2, for example).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to detect multiple subtypes of HBV with mass spectrometry using the Jurinke method since Jurinke expressly teaches "Of interest is also the possibility of determining different HBV subtypes by different masses of the HBV related PCR products (see page 71, column 1)." Norder also expressly motivates subtype detection noting "It is anticipated that PCR technology, including sequencing of amplified fragments, will provide a powerful tool for studying the molecular epidemiology of HBV (see page 220, column 2)." An ordinary practitioner would have been directly motivated by Jurinke to look at different HBV subtypes, including all eight subtypes recognized by Norder, based on the express motivation stated by Jurinke and based upon Norder's express motivation that subtype analysis owuld permit analysis of the epidemiology of HBV and Norder later notes, may also provide information on HIV transmission (see page 220, column 2).

7. Claims 23-26, 30-34, 44-48 and 50-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jurinke et al (Genetic Analysis: Biomolecular Engineering (1996) 13:67-71) in view of Norder et al (J. Med. Virol. (1990) 31:215-221) and further in view of Koster (WO 98/20166).

Jurinke in view of Norder teach the limitations of claims 23-26, 30-34, 45-48 and 51-54 as discussed above. Jurinke suggests analysis in view of Norder do not teach analysis of respiratory pathogens.

Koster expressly teaches analysis of respiratory pathogens such as rhinovirus (see page 74, line 1) as well as influenza virus (see page 74, line 8). Koster also teaches analysis of HIV and HCV (see page 73, line 21 and page 74, line 21). Koster also teaches comparison of base compositions with both modified and unmodified products (see page 66, for example, as well as page 105, table II and pages 69-70). At page 105, table II, Koster provides the base composition of three different PCR products determined by MALDI-TOF. Further, Koster specifically discusses using base composition to analyze mutations as discussed on page 70, where Koster notes "MS can also be used to determined full or partial sequences of larger DNAs; this can be used to detect, locate, and identify new mutations in a given gene region."

In particular, Koster expressly teaches the use of MALDI-TOF for diagnosis of bacterial or viral infections (see pages 73-79). Koster exemplifies this analysis in Example 5.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to utilize the viral targets and mass spectrometry method of Koster in the analytical method of Jurinke in view of Norder since Koster states "In another embodiment, an accurate sequence determination of a relatively large target nucleic acid, can be obtained by generating specifically terminated fragments from the target nucleic acid, determining the mass of each fragment by mass spectrometry and ordering the fragments to determine the sequence of the larger target nucleic acid (see page 75, line 26 to page 76, line 2)." So an ordinary practitioner would have been

motivated to detect the PCR products of Jurinke in view of Norder with the base composition Mass spectrometric approach of Koster since Koster teaches that Mass Spectrometry is accurate and can improve the speed, mass accuracy and precision of the analysis (see abstract, for example).

8. Claim 27 is rejected under 35 U.S.C. 103(a) as being unpatentable over Jurinke et al (Genetic Analysis: Biomolecular Engineering (1996) 13:67-71) in view of Norder et al (J. Med. Virol. (1990) 31:215-221) and further in view of Fuerstanau et al (Rapid Communications in Mass Spectrometry (1995) 9:1528-1538).

Jurinke in view of Norder teach the limitations of claims 23-26, 30-34, 45-48 and 51-54 as discussed above. Jurinke suggests analysis in view of Norder do not teach electrospray ionization with time of flight mass spectrometry.

Fuerstanau teaches analysis of DNA using electrospray ionization and time of flight mass spectrometry (see page 1529, column 1).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to detect to utilize the ES-TOF mass spectrometric method of Fuerstanau in the mass spectrometric analysis of Jurinke in view of Norder since Fuerstanau teaches "It is conceivable that CDMS will find a role in the analysis of a variety of fine particles of biological interest, including DNA fragments and chromosomes, viruses,29 viral DNA, and other cellular constituents as well as entire cells (see page 1537, column 2)." So Fuerstanau expressly teaches analysis of DNA and viruses using ES-TOF and Fuerstanau notes one motivation to select ES-TOF

relative to FTICR since FTICR is complex with costly hardware (see page 1528, column 2, last sentence) while TOF methods are "relatively simple" (see page 1529, column 1). An ordinary practitioner would have been motivated to use ES-TOF in order to use a simple device which would detect DNA and permit analysis of the presence or absence of a virus in a sample as suggested by Jurinke and Fuerstanau.

9. Claims 49 and 55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jurinke et al (Genetic Analysis: Biomolecular Engineering (1996) 13:67-71) in view of Norder et al (J. Med. Virol. (1990) 31:215-221) and further in view of Vanderhallen et al (J. Clin. Microbiol. (1998) 36(12):3463-3467).

Jurinke in view of Norder teach the limitations of claims 23-26, 30-34, 45-48 and 51-54 as discussed above. Jurinke suggests analysis in view of Norder do not teach analysis of polymerase genes.

Vanderhallen teaches analysis of a polymerase gene for typing EMCV (see abstract).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the mass spectrometric approach of Jurinke in view of Norder to type EMCV since Jurinke notes "The detection strategy introduced here has a high potential for automation and represents a fast and reliable method of detection for HBV DNA in serum without the need for time consuming gel electrophoresis and labeling or hybridization procedures (see abstract)." Further, Vanderhallen motivates analysis of the EMCV polymerase noting "The PCR technique

has increased the sensitivity of detection of viral nucleic acids in clinical specimens (see page 3465, column 2)." An ordinary practitioner, interested in improving sensitivity of EMCV detection, would have been motivated to combine the PCR method of Vanderhallen with the mass spectrometric analysis of Jurinke in view of Norder, in order to identify specific subtypes of viruses that are of clinical significance and permit epidemiological tracking of these viruses as taught by Norder.

Response to Arguments

10. Applicant's arguments with respect to the claims have been considered but are moot in view of the new ground(s) of rejection.

Applicant's extensive amendment required the new rejections. The only issue that is remaining is whether Jurinke teaches base composition analysis. As noted in the claim interpretation section above, Jurinke teaches a form of base composition analysis as broadly interpreted. Consequently, the rejection is maintained.

Conclusion

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jeffrey Fredman
Primary Examiner
Art Unit 1637

5/26/06